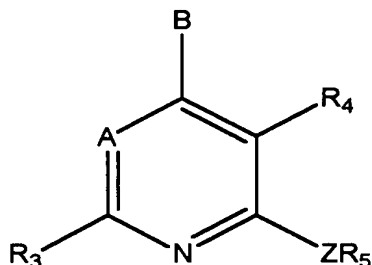




Appendix

1(Amended) A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein

A is N;

B is $-\text{NR}_1\text{R}_2$, $-\text{CR}_1\text{R}_2\text{R}_{11}$, $-\text{C}(=\text{CR}_2\text{R}_{12})\text{R}_1$, $-\text{NHCHR}_1\text{R}_2$, $-\text{OCHR}_1\text{R}_2$, $-\text{SCHR}_1\text{R}_2$, $-\text{CHR}_2\text{OR}_1$, $-\text{CHR}_1\text{OR}_2$, $-\text{CHR}_2\text{SR}_1$, $-\text{C}(\text{S})\text{R}_2$, $-\text{C}(\text{O})\text{R}_2$, $-\text{CHR}_2\text{NR}_1\text{R}_2$, $-\text{CHR}_1\text{NHR}_2$, $-\text{CHR}_1\text{N}(\text{CH}_3)\text{R}_2$, or $-\text{NR}_{12}\text{NR}_1\text{R}_2$;

Y is CH or N;

Z is NH, O, S, ~~$-\text{N}(\text{C}_1\text{-C}_2\text{ alkyl})$~~ , ~~$-\text{NC}(\text{O})\text{CF}_3$~~ , or ~~$-\text{C}(\text{R}_{13}\text{R}_{14})$~~ , ~~$-\text{N}(\text{C}_1\text{-C}_2\text{ alkyl})$~~ , ~~$-\text{NC}(\text{O})\text{CF}_3$~~ , or ~~$-\text{C}(\text{R}_{13}\text{R}_{14})$~~ wherein R_{13} and R_{14} are each, independently, hydrogen, trifluoromethyl or methyl, or one of R_{13} and R_{14} is cyano and the other is hydrogen or methyl, or $-\text{C}(\text{R}_{13}\text{R}_{14})$ is a cyclopropyl group, or Z is nitrogen or CH and forms a five or six membered heterocyclic ring fused with R_5 , which ring optionally comprises two or three further hetero members selected independently from oxygen, nitrogen, NR_{12} , and $\text{S}(\text{O})_m$, and optionally comprises from one to three double bonds, and is optionally substituted with halo, $\text{C}_1\text{-C}_4$ alkyl, $-\text{O}(\text{C}_1\text{-C}_4\text{ alkyl})$, NH_2 , NHCH_3 , $\text{N}(\text{CH}_3)_2$, CF_3 , or OCF_3 , with the proviso that said ring does not contain any $-\text{S-S-}$, $-\text{S-O-}$, $-\text{N-S-}$, or $-\text{O-O-}$ bonds, and does not comprise more than two oxygen or $\text{S}(\text{O})_m$ heterologous members;

R_1 is $\text{C}(\text{O})\text{H}$, $\text{C}(\text{O})(\text{C}_1\text{-C}_6\text{ alkyl hydrocarbyl})$, $\text{C}(\text{O})(\text{C}_1\text{-C}_6\text{ alkylene hydrocarbylene})(\text{C}_3\text{-C}_8\text{ cycloalkyl cyclohydrocarbyl})$, $\text{C}(\text{O})(\text{C}_3\text{-C}_8\text{ cycloalkylene cyclohydrocarbylene})(\text{C}_3\text{-C}_8\text{ cycloalkyl cyclohydrocarbyl})$, $\text{C}(\text{O})(\text{C}_1\text{-C}_6\text{ alkylene hydrocarbylene})(\text{C}_4\text{-C}_8\text{ heterocycloalkyl heterocyclohydrocarbyl})$, $-\text{C}(\text{O})(\text{C}_3\text{-C}_8\text{ cycloalkylene cyclohydrocarbylene})(\text{C}_4\text{-C}_8\text{ heterocycloalkyl heterocyclohydrocarbyl})$, $\text{C}_1\text{-C}_6\text{ alkyl hydrocarbyl}$, $\text{C}_3\text{-C}_8\text{ cycloalkyl cyclohydrocarbyl}$, $\text{C}_4\text{-C}_8\text{ heterocycloalkyl heterocyclohydrocarbyl}$, $-(\text{C}_1\text{-C}_6\text{ alkylene hydrocarbylene})(\text{C}_3\text{-C}_8\text{ cycloalkyl cyclohydrocarbyl})$, $\text{C}_3\text{-C}_8\text{ cycloalkylene}$

cyclohydrocarbylene)(C₃-C₈ cycloalkyl cyclohydrocarbyl), -(C₁-C₆ alkylene hydrocarbylene)(C₄-C₈ heterocycloalkyl heterocyclohydrocarbyl), -(C₃-C₈ cycloalkylene cyclohydrocarbylene)(C₄-C₈ heterocycloalkyl heterocyclohydrocarbyl), or -O-aryl, or -O-(C₁-C₆ alkylene hydrocarbylene)-aryl; wherein said aryl, C₄-C₈ heterocycloalkyl heterocyclohydrocarbyl, C₁-C₆ alkyl hydrocarbyl, C₃-C₈ cycloalkyl cyclohydrocarbyl, C₃-C₈ cycloalkylene cyclohydrocarbylene, and C₁-C₆ alkylene hydrocarbylene groups may each independently be optionally substituted with from one to six fluoro and may each independently be optionally substituted with one or two substituents R₈ independently selected from the group consisting of C₁-C₄ alkyl hydrocarbyl, -C₃-C₈ cycloalkyl cyclohydrocarbyl, hydroxy, chloro, bromo, iodo, CF₃, -O-(C₁-C₆ alkyl hydrocarbyl), -O-(C₃-C₅ cycloalkyl cyclohydrocarbyl), -O-CO-(C₁-C₄ alkyl hydrocarbyl), -O-CO-NH(C₁-C₄ alkyl hydrocarbyl), -O-CO-N(R₂₄)(R₂₅), -N(R₂₄)(R₂₅), -S(C₁-C₄ alkyl hydrocarbyl), -S(C₃-C₅ cycloalkyl cyclohydrocarbyl) -N(C₁-C₄ alkyl hydrocarbyl)CO(C₁-C₄ alkyl hydrocarbyl), -NHCO(C₁-C₄ alkyl hydrocarbyl), -COO(C₁-C₄ alkyl hydrocarbyl), -CONH(C₁-C₄ alkyl hydrocarbyl), -CONC₁-C₄ alkyl hydrocarbyl)(C₁-C₂ alkyl hydrocarbyl), CN, NO₂, -OSO₂(C₁-C₄ alkyl hydrocarbyl), S⁺(C₁-C₆ alkyl hydrocarbyl)(C₁-C₂ alkyl hydrocarbyl), -SO(C₁-C₄ alkyl hydrocarbyl) and -SO₂(C₁-C₄ alkyl hydrocarbyl); and wherein the C₁-C₆ alkyl hydrocarbyl, C₁-C₆ alkylene hydrocarbylene, C₃-C₈ cycloalkyl cyclohydrocarbyl, C₃-C₈ cycloalkylene cyclohydrocarbylene, and C₃-C₈ heterocycloalkyl heterocyclohydrocarbyl moieties of R₁ may optionally independently contain from one to three double or triple bonds; and wherein the C₁-C₄ alkyl hydrocarbyl moieties and C₁-C₆ alkyl hydrocarbyl moieties of R₈ can optionally independently be substituted with hydroxy, amino, C₁-C₄ alkyl, aryl, -CH₂-aryl, C₃-C₅ cycloalkyl, or -O-(C₁-C₄ alkyl), and can optionally independently be substituted with from one to six fluoro, and can optionally contain one or two double or triple bonds; and wherein each heterocycloalkyl heterocyclohydrocarbyl group of R₁ contains from one to three heteromoieties selected from oxygen, S(O)_m, nitrogen, and NR₁₂;

R₂ is hydrogen, C₁-C₁₂ alkyl hydrocarbyl, C₃-C₈ cycloalkyl cyclohydrocarbyl, C₄-C₈ heterocycloalkyl heterocyclohydrocarbyl, -(C₁-C₆ alkylene hydrocarbylene)(C₃-C₈ cycloalkyl cyclohydrocarbyl), -(C₃-C₈ cycloalkylene cyclohydrocarbylene)(C₃-C₈ cycloalkyl cyclohydrocarbyl), -(C₁-C₆ alkylene hydrocarbylene)(C₄-C₈ heterocycloalkyl heterocyclohydrocarbyl), -(C₃-C₆ cycloalkylene cyclohydrocarbylene)(C₄-C₈ heterocycloalkyl

heterocyclohydrocarbyl), aryl, -(C₁-C₆ alkylene hydrocarbylene)aryl, or -(C₃-C₈ cycloalkylene cyclohydrocarbylene)(aryl); wherein each of the foregoing R₂ groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro, and C₁-C₆ alkyl, wherein one of said one to three substituents can further be selected from bromo, iodo, C₁-C₆ alkoxy, -OH, -O-CO-(C₁-C₆ alkyl), -O-CO-N(C₁-C₄ alkyl)(C₁-C₂ alkyl), -S (C₁-C₆ alkyl), -S(O)(C₁-C₆ alkyl), -S(O)₂(C₁-C₆ alkyl), S⁺(C₁-C₆ alkyl)(C₁-C₂ alkyl)I', CN, and NO₂; and wherein the C₁-C₁₂ alkyl hydrocarbyl, -(C₁-C₆ alkylene hydrocarbylene), -(C₃-C₈ cycloalkyl), -(C₃-C₈ cycloalkylene), and -(C₃-C₈ heterocycloalkyl) and cyclohydrocarbyl groups of 5 - 8 carbon atoms, cyclohydrocarbylene groups of 5 to 8 carbon atoms and heterocyclohydrocarbyl groups of 5 to 8 atoms moieties of R₂ may optionally independently contain from one to three double or triple bonds; and wherein each heterocycloalkyl heterocyclohydrocarbyl group of R₂ contains from one to three heteromoiety selected from oxygen, S(O)_m, nitrogen, and NR₁₂;

or when R₁ and R₂ are as in -NHCHR₁R₂, -OCHR₁R₂, -SCHR₁R₂, -CHR₁R₂ or -NR₁R₂, R₁ and R₂ of B may form a saturated 5- to 8-membered ring which may optionally contain one or two double bonds and in which one or two of the ring carbons may optionally be replaced by an oxygen, S(O)_m, nitrogen or NR₁₂; and which carbocyclic ring can optionally be substituted with from 1 to 3 substituents selected from the group consisting of hydroxy, C₁-C₄ alkyl, fluoro, chloro, bromo, iodo, CF₃, -O-(C₁-C₄ alkyl), -O-CO-(C₁-C₄ alkyl), -O-CO-NH(C₁-C₄ alkyl), -O-CO-N(C₁-C₄ alkyl)(C₁-C₂ alkyl), -NH(C₁-C₄ alkyl), -N(C₁-C₂ alkyl)(C₁-C₄ alkyl), -S(C₁-C₄ alkyl), -N(C₁-C₄ alkyl)CO(C₁-C₄ alkyl), -NHCO(C₁-C₄ alkyl), -COO(C₁-C₄ alkyl), -CONH(C₁-C₄ alkyl), -CON(C₁-C₄ alkyl)(C₁-C₂ alkyl), CN, NO₂, -OSO₂(C₁-C₄ alkyl), -SO(C₁-C₄ alkyl), and -SO(C₁-C₄ alkyl), wherein one of said one to three substituents can further be selected from phenyl;

R₃ is methyl, ethyl, fluoro, chloro, bromo, iodo, cyano, methoxy, OCF₃, NH₂, NH(C₁-C₂ alkyl), N(CH₃)₂, -NHCOCF₃, -NHCH₂CF₃, S(O)_m(C₁-C₄ alkyl), CONH₂, -CONHCH₃, CON(CH₃)₂, -CF₃, or CH₂OCH₃;

R₄ is hydrogen, C₁-C₄ alkyl hydrocarbyl, C₃-C₅ cycloalkyl, -(C₁-C₄ alkylene hydrocarbylene)(C₃-C₅ cycloalkyl), -(C₃-C₅ cycloalkylene)(C₃-C₆ cycloalkyl), cyano, fluoro, chloro, bromo, iodo, -OR₂₄, C₁-C₆ alkoxy, -O- cycloalkyl, -O-(C₁-C₄ alkylene hydrocarbylene)(C₃-C₅ cycloalkyl), -O-(C₃-C₅ cycloalkylene)(C₃-C₅ cycloalkyl), -CH₂SC(S)O(C₁-C₄ alkyl), -CH₂OF₃, CH₂OCF₃, CF₃, amino, nitro, -NR₂₄R₂₅, -(C₁-C₄ alkylene

hydrocarbylene)-OR₂₄, -(C₁-C₄ alkylene hydrocarbylene)Cl, -(C₁-C₄ alkylene hydrocarbylene)NR₂₄R₂₅, -NHCOR₂₄, -NHCONR₂₄R₂₅, -C=NOR₂₄, -CH=NOR₂₄, -NHNOR₂₄R₂₅, -S(O)_mR₂₄, -C(O)R₂₄, -OC(O)R₂₄, -C(O)CN, -C(O)NR₂₄R₂₅, -C(O)NHNOR₂₄R₂₅, and -COOR₂₄, wherein the alkyl hydrocarbyl and alkylene hydrocarbylene groups of R₄ may optionally independently contain one or two double or triple bonds and may optionally independently be substituted with one or two substituents R₁₀ independently selected from hydroxy, amino, -NHCOCH₃, -NHCOCH₂Cl, -NH(C₁-C₂ alkyl), -N(C₁-C₂ alkyl)(C₁-C₂ alkyl), -COO(C₁-C₄ alkyl), -COOH, -CO(C₁-C₄ alkyl), C₁-C₆ alkoxy, C₁-C₃ thioalkyl, cyano and nitro, and with one to four substituents independently selected from fluoro and chloro;

R₅ is aryl or heteroaryl and is substituted with from one to four substituents R₂₇ independently selected from halo, C₁-C₁₀ alkyl hydrocarbyl, -(C₁-C₄ alkylene hydrocarbylene)(C₃-C₈ cycloalkyl), -(C₁-C₄ alkylene hydrocarbylene)(C₄-C₈ heterocycloalkyl), -(C₃-C₈ cycloalkyl), -(C₄-C₈ heterocycloalkyl), -(C₃-C₈ cycloalkylene)(C₃-C₈ cycloalkyl), -(C₃-C₈ cycloalkylene)(C₄-C₈ heterocycloalkyl), C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, nitro, cyano, -NR₂₄R₂₅, -NR₂₄COR₂₅, -NR₂₄CO₂R₂₆, -COR₂₄, -OR₂₅, -CONR₂₄R₂₅, -CO(NOR₂₂)R₂₃, -CON(OR₂₂)R₂₃, -CO₂R₂₆, -C=N(OR₂₂)R₂₃, and -S(O)_mR₂₃; wherein said C₁-C₁₀ alkyl, C₃-C₈ cycloalkyl, (C₁-C₄ alkylene hydrocarbylene), (C₃-C₈ cycloalkyl), (C₃-C₈ cycloalkylene), and (C₄-C₈ heterocycloalkyl) groups can be optionally substituted with from one to three substituents independently selected from C₁-C₄ alkyl, C₃-C₈ cycloalkyl, (C₁-C₄ alkylene hydrocarbylene)(C₃-C₈ cycloalkyl), -(C₃-C₈ cycloalkylene)(C₃-C₈ cycloalkyl), C₁-C₄ haloalkyl, hydroxy, C₁-C₆ alkoxy, nitro, halo, cyano, -NR₂₄R₂₅, -NR₂₄COR₂₅, -NR₂₄CO₂R₂₆, -COR₂₄, -OR₂₅, -CONR₂₄R₂₅, CO₂R₂₆, -CO(NOR₂₂)R₂₅, and -S(O)_mR₂₃; and wherein two adjacent substituents of the R₅ group can optionally form a 5-7 membered ring, saturated or unsaturated, fused to-R⁵ R₅, which ring optionally can contain one, two, or three heterologous members independently selected from O, S(O)_m, and N, but not any -S-S-, -O-O-, -S-O-, or -N-S- bonds, and which ring is optionally substituted with C₁-C₄ alkyl, C₃-C₈ cycloalkyl, -(C₁-C₄ alkylene)(C₃-C₈ cycloalkyl), -(C₃-C₈ cycloalkylene)(C₃-C₈ cycloalkyl), C₁-C₄ haloalkyl, nitro, halo, cyano, -NR₂₄R₂₅, -NR₂₄COR₂₅, -NR₂₄CO₂R₂₆, -COR₂₄, -OR₂₅, -CONR₂₄R₂₅, CO₂R₂₆, -CO(NOR₂₂)R₂₅, or -S(O)_mR₂₃; wherein one of said one to four optional substituents R₂₇, can further be selected from -SO₂NH(C₁-C₄ alkyl), -SO₂NH(C₁-C₄ alkylene)(C₃-C₈ cycloalkyl), SO₂NH(C₃-C₈ cycloalkyl), -SO₂NH(C₃-C₈ cycloalkylene)(C₃-C₈ cycloalkyl), -SO₂N(C₁-C₄ alkyl)(C₁-C₂ alkyl), -SO₂NH₂, -NHCO₂(C₁-C₄ alkyl), -NHCO₂(C₃-C₈ cycloalkyl), -NHCO₂(C₁-C₄ alkylene)(C₃-C₈ cycloalkyl), and -NHCO₂(C₃-C₈ cycloalkylene)(C₃-C₈ cycloalkyl); and wherein the alkyl hydrocarbyl, and alkylene hydrocarbylene groups of R₅ may independently optionally contain one double or triple bond;

R₁₁ is hydrogen, hydroxy, fluoro, ethoxy, or methoxy;

R₁₂ is hydrogen or C₁-C₄ alkyl;

R₂₂ is independently at each occurrence selected from hydrogen, C₁-C₄ alkyl, C₃-C₈ haloalkyl, C₃-C₆ alkenyl, C₃-C₆ alkynyl, C₃-C₈ cycloalkyl, (C₃-C₈ cycloalkylene)(C₃-C₈ cycloalkyl), and (C₁-C₄ alkylene)(C₃-C₈ cycloalkyl);

R₂₂ is independently at each occurrence selected from hydrogen, C₁-C₁₄ alkyl, C₁-C₁₄ haloalkyl, C₃-C₆ alkenyl, C₃-C₆ alkynyl, C₃-C₈ cycloalkyl, (C₃-C₈ cycloalkylene)(C₃-C₈ cycloalkyl), and (C₁-C₄ alkylene)(C₃-C₈ cycloalkyl);

R₂₃ is independently at each occurrence selected from C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₂-C₈ alkoxyalkyl, C₃-C₈ cycloalkyl, -(C₁-C₄ alkylene)(C₃-C₈ cycloalkyl), -(C₃-C₈ cycloalkylene)(C₃-C₈ cycloalkyl), aryl, -(C₁-C₄ alkylene)aryl, piperidine, pyrrolidine, piperazine, N-methylpiperazine, morpholine, and thiomorpholine;

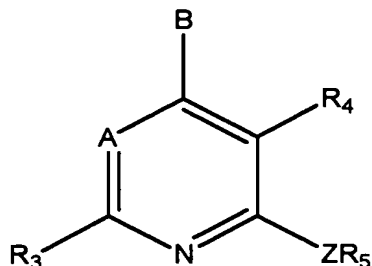
R₂₄ and R₂₅ are independently at each occurrence selected from hydrogen, -C₁-C₄ alkyl, C₁-C₄ haloalkyl, ~~especially CF₃, -CHF₂, -CF₂CF₃, or -CH₂CF₃~~, -(C₁-C₄ alkylene)OH, -(C₁-C₄ alkylene)-O-(C₁-C₄ alkyl), -(C₁-C₄ alkylene)-O-(C₃-C₅ cycloalkyl), C₃-C₈ cycloalkyl, -(C₁-C₄ alkylene)(C₃-C₈ cycloalkyl), -(C₃-C₈ cycloalkylene)(C₃-C₈ cycloalkyl), -C₄-C₈ ~~heterocycloalkyl~~ heterocyclohydrocarbyl, -(C₁-C₄ alkylene)(C₄-C₈ ~~heterocycloalkyl~~ heterocyclohydrocarbyl), -(C₃-C₈ cycloalkylene)(C₄-C₈ ~~heterocycloalkyl~~ heterocyclohydrocarbyl), aryl, and -(C₁-C₄ alkylene)(aryl), wherein the -C₄-C₈ ~~heterocycloalkyl~~ heterocyclohydrocarbyl groups can each independently optionally be substituted with aryl, CH₂-aryl, or C₁-C₄ alkyl, and can optionally contain one or two double or triple bonds; or, when R₂₄ and R₂₅ are as NR₂₄R₂₅, -C(O)NR₂₄R₂₅, -(C₁-C₄ alkylene)NR₂₄R₂₅, or -NHCONR₂₄R₂₅, then NR₂₄R₂₅ may further optionally form a 4 to 8 membered heterocyclic ring optionally containing one or two further hetero members independently selected from S(O)_m, oxygen, nitrogen, and NR₁₂, and optionally containing from one to three double bonds;

R₂₆ is independently at each occurrence selected from C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₃-C₈ cycloalkyl, -(C₁-C₄ alkylene)(C₃-C₈ cycloalkyl), -(C₃-C₈ cycloalkylene)(C₃-C₈ cycloalkyl), aryl, and -(C₁-C₄ alkylene)(aryl); and

wherein each m is independently zero, one, or two,

with the proviso that ~~heterocycloalkyl~~ heterocyclohydrocarbylene groups of the compound of formula-I, ~~H~~, or ~~II~~ do not comprise any -S-S-, -S-O-, -N-S-, or -O-O- bonds, and do not comprise more than two oxygen or S(O)_m heterologous members.

2. A compound according to claim 1 of the formula



or a pharmaceutically acceptable salt thereof, wherein

A is N;

B is $-NR_1R_2$, $-CR_1R_2R_{11}$, $-C(=CR_2R_{12})R_1$, $-NHCHR_1R_2$, $-OCHR_1R_2$, $-SCHR_1R_2$, $-CHR_2OR_{12}$, $-CHR_2SR_{12}$, $-C(S)R_2$ or $-C(O)R_2$;

Z is $-NH$, O, S, $N(C_1-C_2 \text{ alkyl})$ or $C(R_{13}R_{14})$ wherein R_{13} and R_{14} are each independently, hydrogen, trifluoromethyl or methyl or one of R_{13} and R_{14} is cyano and the other is hydrogen or methyl;

R_1 is C_1-C_6 alkyl hydrocarbyl which may optionally be substituted with one or two substituents R_8 independently selected from the group consisting of hydroxy, fluoro, chloro, bromo, iodo, CF_3 , C_1-C_4 alkoxy, $-O-CO-(C_1-C_4 \text{ a } \text{alkyl hydrocarbyl})$, $-O-CO-NH(C_1-C_4 \text{ alkyl hydrocarbyl})$, $-O-CO-N(C_1-C_4 \text{ alkyl hydrocarbyl})(C_1-C_2 \text{ alkyl hydrocarbyl})$, $-NH(C_1-C_4 \text{ alkyl hydrocarbyl})$, $-N(C_1-C_2 \text{ alkyl})(C_1-C_4 \text{ alkyl hydrocarbyl})$, $-S(C_1-C_4 \text{ alkyl})$, $-N(C_1-C_4)CO(C_1-C_4 \text{ alkyl hydrocarbyl})$, $-NHCO(C_1-C_4 \text{ alkyl hydrocarbyl})$, $-COO(C_1-C_4 \text{ alkyl hydrocarbyl})$ alkyl hydrocarbyl, $-CONH(C_1-C_4 \text{ alkyl hydrocarbyl})$, $-CON(C_1-C_4 \text{ alkyl hydrocarbyl})(C_1-C_2 \text{ alkyl})$, CN , NO_2 , $-SO(C_1-C_4 \text{ alkyl hydrocarbyl})$ and $-SO_2(C_1-C_4 \text{ alkyl hydrocarbyl})$, and wherein said C_1-C_6 alkyl hydrocarbyl and the $(C_1-C_4) \text{ alkyl hydrocarbyl}$ moieties in the foregoing R_1 groups may optionally contain one carbon-carbon double or triple bond;

R_2 is C_1-C_{12} alkyl hydrocarbyl, aryl or $-(C_1-C_4 \text{ alkylene hydrocarbylene})$ aryl wherein said aryl is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, benzisothiazolyl, benzisoxazolyl, benzimidazolyl, indolyl, or benzoxazolyl; 3- to 8-membered cycloalkyl or $-(C_1-C_6 \text{ alkylene})$ cycloalkyl, wherein one or two of the ring carbons of said cycloalkyl having at least 4 ring members and the cycloalkyl moiety of said $-(C_1-C_6 \text{ alkylene})$ cycloalkyl having at least 4 ring members may optionally be replaced by an oxygen or sulfur atom or by $N-R_9$ wherein R_9 is hydrogen or C_1-C_4 alkyl; and wherein each of the foregoing R_2 groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro and C_1-C_4 alkyl, or with one substituent selected from bromo, iodo, C_1-C_6 alkoxy, $-O-CO-(C_1-C_6$

alkyl), -O-CO-N(C₁-C₄ alkyl)(C₁-C₂ alkyl), -S(C₁-C₆ alkyl), CN, NO₂, -SO(C₁-C₄ alkyl), and -SO₂(C₁-C₄ alkyl), and wherein said C₁-C₁₂ ~~alkyl~~ hydrocarbyl and the C₁-C₄ ~~alkylene~~ hydrocarbylene moiety of said -(C₁-C₄ ~~alkylene~~ hydrocarbylene)aryl may optionally contain one carbon-carbon double or triple bond;

or -NR₁R₂ or -CR₁R₂R₁₁ may form a saturated 5- to 8-membered carbocyclic ring which may optionally contain one or two carbon-carbon double bonds and in which one or two of the ring carbons may optionally be replaced by an oxygen or sulfur atom;

R₃ is methyl, ethyl, fluoro, chloro, bromo, iodo, cyano, methoxy, OCF₃, methylthio, methylsulfonyl, CH₂OH, or CH₂OCH₃;

R₄ is hydrogen, C₁-C₄ ~~alkyl~~ hydrocarbyl, fluoro, chloro, bromo, iodo, C₁-C₄ alkoxy, trifluoromethoxy, -CH₂OCH₃, -CH₂OCH₂CH₃, -CH₂CH₂OCH₃, -CH₂OF₃, CF₃, amino, nitro, -NH(C₁-C₄ alkyl), -N(CH₃)₂, -NHCOCH₃, -NHCONHCH₃, -SO_n(C₁-C₄ ~~alkyl~~ hydrocarbyl) wherein n is 0, 1 or 2, cyano, hydroxy, -CO(C₁-C₄ ~~alkyl~~ hydrocarbyl), -CHO, cyano or -COO(C₁-C₄ alkyl) wherein said C₁-C₄ ~~alkyl~~ hydrocarbyl may optionally contain one double or triple bond and may optionally be substituted with one substituent selected from hydroxy, amino, -NHCOCH₃, -NH(C₁-C₂ alkyl), -N(C₁-C₂ alkyl)₂, -COO(C₁-C₄ alkyl), -CO(C₁-C₄ alkyl), C₁-C₃ alkoxy, C₁-C₃ thioalkyl, fluoro, chloro, cyano and nitro;

R₅ is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidyl, furanyl, benzofuranyl, benzothiazolyl, or indolyl, wherein each of the above groups R₅ is substituted with from one to three substituents independently selected from fluoro, chloro, C₁-C₆ alkyl, and C₁-C₆ alkoxy, or with one substituent selected from hydroxy, iodo, bromo, formyl, cyano, nitro, trifluoromethyl, amino, -(C₁-C₆ alkyl)O(C₁-C₆)alkyl, -NHCH₃, -N(CH₃)₂, -COOH, -COO(C₁-C₄ alkyl), -CO(C₁-C₄ alkyl), -SO₂NH(C₁-C₄ alkyl), -SO₂N(C₁-C₄ alkyl)(C₁-C₂ alkyl), -SO₂NH₂, -NHSO₂(C₁-C₄ alkyl), -S(C₁-C₆ alkyl) and -SO₂(C₁-C₆ alkyl), and wherein the C₁-C₄ alkyl and C₁-C₆ alkyl moieties of the foregoing R₅ groups may optionally be substituted with one or two fluoro groups or with one substituent selected from hydroxy, amino, methylamino, dimethylamino and acetyl;

R₁₁ is hydrogen, hydroxy, fluoro, or methoxy;

R₁₂ is hydrogen or C₁-C₄ alkyl; and

or a pharmaceutically acceptable salt of such compound.

3. (Amended) A compound according to claim 2 wherein B is -NR₁R₂, -NHCHR₁R₂, -SCHR₁R₂ or -OCHR₁R₂; R₁ is C₁-C₆ ~~alkyl~~ hydrocarbyl, which may optionally be substituted with one hydroxy, fluoro, CF₃, or C₁-C₂ alkoxy group and may optionally contain one double or triple bond; and R₂ is benzyl or C₁-C₆ ~~alkyl~~ hydrocarbyl which may optionally contain one

carbon-carbon double or triple bond, wherein said C₁-C₆ alkyl or the phenyl moiety of said benzyl may optionally be substituted with fluoro, CF₃, C₁-C₂ alkyl, or C₁-C₂ alkoxy.

4. (Amended) A compound according to claim 2 wherein R₁ is C₁-C₆ ~~alkyl~~ hydrocarbyl which may be substituted by fluoro, CF₃, hydroxy, C₁-C₂ alkyl or C₁-C₂ alkoxy and which may optionally contain one carbon-carbon double or triple bond.

13. (Amended) A pharmaceutical composition for the treatment of (a) a disorder or condition the treatment of which can be effected or facilitated by antagonizing CRF, ~~including but not limited to disorders induced or facilitated by CRF~~, or (b) a disorder or condition selected from inflammatory disorders ~~such as rheumatoid arthritis and osteoarthritis~~, pain, asthma, psoriasis and allergies; generalized anxiety disorder; panic; phobias, ~~including social phobia, agoraphobia, and specific phobias~~; obsessive-compulsive disorder; post-traumatic stress disorder; sleep disorders induced by stress; pain perception ~~such as fibromyalgia~~; mood disorders ~~such as depression, including major depression, single episode depression, recurrent depression, child abuse induced depression~~, mood disorders associated with premenstrual syndrome, and postpartum depression; dysthemia; bipolar disorders; cyclothymia; chronic fatigue syndrome; stress-induced headache; cancer; irritable bowel syndrome, Crohn's disease; spastic colon; post operative ileus; ulcer; diarrhea; stress-induced fever; human immunodeficiency virus infections; neurodegenerative diseases ~~such as Alzheimer's disease, Parkinson's disease and Huntington's disease~~; gastrointestinal diseases; eating disorders such as anorexia and bulimia nervosa; hemorrhagic stress; chemical dependencies or addictions, ~~including dependencies or addictions to alcohol, cocaine, heroin, benzodiazapines, or other drugs~~; drug or alcohol withdrawal symptoms; stress-induced psychotic episodes; euthyroid sick syndrome; syndrome of inappropriate antidiuretic hormone; obesity; infertility; head trauma; spinal cord trauma; ischemic neuronal damage, including cerebral ischemia, ~~for example cerebral hippocampal ischemia, excitotoxic neuronal damage~~; epilepsy; stroke; immune dysfunctions including stress induced immune dysfunctions, ~~including porcine stress syndrome, bovine shipping fever, equine paroxysmal fibrillation, confinement dysfunction in chicken, sheering stress in sheep, and human animal interaction stress in dogs~~; muscular spasms; urinary incontinence; senile dementia of the Alzheimer's type; multi infarct dementia; amyotrophic lateral sclerosis; hypertension; tachycardia; congestive heart failure; osteoporosis; premature birth; hypoglycemia, and Syndrome X in a mammal or bird, comprising an amount of a compound according to claim 1 that is effective in the treatment of such disorder or condition, and a pharmaceutically acceptable carrier.

14. A pharmaceutical composition according to claim 13 for the treatment of a disorder selected from inflammatory disorders ~~such as rheumatoid arthritis and osteoarthritis~~, pain, asthma, psoriasis and allergies; generalized anxiety disorder; panic; phobias; obsessive compulsive disorder; post-traumatic stress disorder; sleep disorders induced by stress; pain perception ~~such as fibromyalgia~~; mood disorders such as depression, ~~including major depression, single episode depression, recurrent depression, child abuse induced depression~~, and postpartum depression; dysthemia; bipolar disorders; cyclothymia; fatigue syndrome; stress induced headache; cancer; irritable bowel syndrome, Crohn's disease; spastic colon; human immunodeficiency virus (HIV) infections; neurodegenerative diseases ~~such as Alzheimer's disease, Parkinson's disease and Huntington's disease~~; gastrointestinal diseases; eating disorders ~~such as anorexia and bulimia nervosa~~; ~~hemorrhagic stress~~; chemical dependencies and addictions; obesity; infertility; head traumas; spinal cord trauma; ischemic neuronal damage; excitotoxic neuronal damage; epilepsy; stroke; immune dysfunctions ~~including stress induced immune dysfunctions~~; muscular spasms; urinary incontinence; senile dementia of the Alzheimer's type; multi infarct dementia; amyotrophic lateral sclerosis; and hypoglycemia in a mammal, including a human.